

### Remarks

Applicants have received and reviewed the Office Action mailed November 2, 2001. By way of response, Applicants have amended claims 24 and 35 and present new claims 45-67. Claims 24-67 are now pending. No new matter is introduced. Applicants submit that the amended and newly presented claims are supported by the specification.

Applicants appreciate and acknowledge the withdrawal of rejections under 35 U.S.C. § 112(1) and 112(2).

For the reasons given below, Applicants respectfully submit that the amended and newly presented claims are in condition for allowance, and notification to that effect is earnestly solicited.

### Petition for Extension of Time

It is noted that a three-month petition for extension of time is necessary to provide for timeliness of the response. A request for such an extension is made extending the time for response from February 2, 2002 to May 2, 2002.

### 35 U.S.C. § 112, First Paragraph Rejections

The Examiner rejected claims 24-44 under 35 U.S.C. § 112, first paragraph. The Office Action asserts that the claims must be limited to specifically exemplified single and double mutations. Although this rejection has not been raised for the newly presented claims, it is discussed insofar as it might apply. Applicants respectfully traverse this rejection.

### Newly Presented Claims 45-67

The Office Action objected to claims that recite three or more amino acid substitutions. The Office Action also suggested that claims reciting exemplified embodiments of the present SPE-C mutants might be allowable.

Regarding triple mutants, Applicants respectfully draw the Examiner's attention to Example 5, which specifically describes making triple mutants of SPE-C. One triple mutant embodiment of SPE-C that is supported by the disclosure of the present specification is described in the Declaration Under 37 C.F.R. § 1.132 by Patrick M. Schlievert, which was one of two

Declarations submitted in the present application on March 7, 2000. Thus, triple mutants are exemplified in and supported by the present application.

Claims 45-58 recite one, two, or three amino acid substitutions in SPE-C. The dependent claims recite specific, exemplified substitutions.

Claims 59-67 recite only substitutions at positions shown in the examples to provide desirable properties for the SPE-C mutants. The dependent claims recite specific, exemplified positions and substitutions.

Accordingly, it is believed that claims 45-67 do not include any of the recitations objected to in the Office Action.

#### **Claims 24-44**

Applicants maintain that the facts, authority, and reasoning presented in their submissions mailed March 6, 2000, November 11, 2000, and August 8, 2001 address the Examiner's comments regarding claims 24-44.

Applicants respectfully request that the Examiner reconsider the rejection of claims 24-44 in light of the support in the present specification. The specific factual support found in the specification was pointed out at pages 6-8 of the Preliminary Amendment mailed August 8, 2001 and at pages 6-7 of the Amendment & Response mailed November 11, 2000. Examples supporting the claims are found in the present application and in the Declaration Under 37 C.F.R. § 1.132 by Patrick M. Schlievert mailed March 7, 2000.

Applicants read the current rejection as requiring that the claims be limited to only the exemplified embodiments. Applicants presented in the Amendment mailed March 6, 2000 an extensive discussion indicating that such a rejection is improper. This discussion employed the authority found in the MPEP and the case law together with the facts presented in the present specification. Applicants respectfully request that the Examiner reconsider this authority as it applies to claims 24-44. In particular, the paragraph bridging pages 5 and 6 and the last two paragraphs on page 6 (the second bridging page 7) of that Amendment address the severity of limiting claims to exemplified embodiments.

Applicants would also like to address the comments in the Office Action regarding stability of the mutants. The Office Action asserts that the specification does not provide guidance on how multiple amino acids can be deleted, substituted, or inserted for the production

of a stable protein. Applicants respectfully disagree regarding the relevancy of protein stability for this invention. As pointed out in the Amendment mailed March 6, 2000, for a vaccine, the mutant is advantageously nonlethal. The protein does not have to be stable and remain intact to function as a vaccine. There is support for claims that the mutants can be used as vaccines. Two double mutants (Y15A/N38A and Y17A/N38A) were prepared as described in Example 5 and then evaluated in Example 6. The mutations were effective as vaccines. Finally, there are no claims in the present invention regarding the stability of the mutations.

## **Conclusion**

Accordingly, it is submitted that claims 24-67 fully comply with § 112, first paragraph, and withdrawal of this rejection is respectfully requested.

## **35 U.S.C. § 112, Second Paragraph Rejections**

The Examiner rejected claim 24-44 under 35 U.S.C. § 112, second paragraph. The Office Action objects to the recitation of "substantially nonlethal" in claims 24 and 35.

Applicants respectfully submit that the phrase "substantially nonlethal" is defined in the specification at least at page 17, lines 10-12. This passage states that, "A mutant SPE-C toxin or fragment thereof is substantially nonlethal if when administered to a rabbit at the same dose as the wild type toxin less than about 10-20% of rabbits die." It is believed that a claim reciting "nonlethal" rather than "substantially nonlethal" has a nearly identical meaning. Accordingly, claims 24 and 35 have been amended to delete the term "substantially". This renders this rejection moot.

Accordingly, it is submitted that claims 24-67 fully comply with § 112, second paragraph, and withdrawal of this rejection is respectfully requested.

**Summary**

In summary, Applicants assert that each of claims 24-67 are in condition for allowance, and notification of that effect is earnestly solicited.

The Examiner is invited to contact Applicants' undersigned representative at the telephone number provided below, if the Examiner believes that doing so will expedite prosecution of the application.

Respectfully submitted,

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MARKED-UP VERSION TO SHOW CHANGES MADE

24. (Amended) A mutant Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising:

an amino acid substitution of aspartic acid-12, tyrosine-15, tyrosine-17, histidine-35, asparagine-38, or substitution at more than one of these amino acids; and

wherein the mutant is [substantially] nonlethal compared with a wild type SPE-C toxin.

35. (Amended) A mutant SPE-C toxin comprising:

an amino acid substitution of aspartic acid-12 to alanine, glutamic acid, asparagine, glutamine, lysine, arginine, serine, or threonine;

an amino acid substitution of tyrosine-15 to phenylalanine, alanine, glycine, serine, or threonine;

an amino acid substitution of tyrosine-17 to phenylalanine, alanine, glycine, glutamic acid, lysine, arginine, aspartic acid, serine, or threonine;

an amino acid substitution of histidine-35 to phenylalanine, alanine, glycine, glutamic acid, lysine, arginine, aspartic acid, tyrosine, phenylalanine, serine, or threonine;

an amino acid substitution of asparagine-38 to alanine, aspartic acid, glutamic acid, lysine or arginine; or

substitution at more than one of these amino acids; and

wherein the mutant is [substantially] nonlethal compared with a wild type SPE-C toxin.